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## NOTICE OF ALLOWANCE AND FEE(S) DUE

24392 7590 12/30/2008

FISH & ASSOCIATES, PC  
ROBERT D. FISH  
2603 Main Street  
Suite 1050  
Irvine, CA 92614-6232

EXAMINER

WOOLWINE, SAMUEL C

ART UNIT

PAPER NUMBER

1637

DATE MAILED: 12/30/2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,284	04/21/2005	Eric Fredericus Bernardus Thunnissen	13634PCTUS	1854
TITLE OF INVENTION: HUMAN PAPILLOMA VIRUS DETECTION WITH DNA MICROARRAY				

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$755	\$300	\$0	\$1055	03/30/2009

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. **PROSECUTION ON THE MERITS IS CLOSED.** THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN **THREE MONTHS** FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. **THIS STATUTORY PERIOD CANNOT BE EXTENDED.** SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

## HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER:** Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

# **PART B - FEE(S) TRANSMITTAL**

**Complete and send this form, together with applicable fee(s), to:** Mail **Mail Stop ISSUE FEE**  
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**P.O. Box 1450**  
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 or Fax **(571)-273-2885**

**INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

24392 7590 12/30/2008

**FISH & ASSOCIATES, PC**  
**ROBERT D. FISH**  
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**Suite 1050**  
**Irvine, CA 92614-6232**

## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/511,284 04/21/2005 Eric Fredericus Bernardus Thunnissen 13634PCT/US 1854

**TITLE OF INVENTION: HUMAN PAPILLOMA VIRUS DETECTION WITH DNA MICROARRAY**

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$755	\$300	\$0	\$1055	03/30/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
WOOLWINE, SAMUEL C	1637	435-006000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.  
☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a **Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_  
 (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 \_\_\_\_\_  
 3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee  
☐ Publication Fee (No small entity discount permitted)  
☐ Advance Order - # of Copies \_\_\_\_\_

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.  
☐ Payment by credit card. Form PTO-2038 is attached.  
☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

5. **Change in Entity Status** (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_ Date \_\_\_\_\_  
 Typed or printed name \_\_\_\_\_ Registration No. \_\_\_\_\_

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.**

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24392	7590	12/30/2008	EXAMINER	
FISH & ASSOCIATES, PC ROBERT D. FISH 2603 Main Street Suite 1050 Irvine, CA 92614-6232			WOOLWINE, SAMUEL C.	
			ART UNIT	PAPER NUMBER
			1637	
			DATE MAILED: 12/30/2008	

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 319 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 319 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

**Notice of Allowability****Application No.**

10/511,284

**Examiner**

SAMUEL WOOLWINE

**Applicant(s)**

THUNNISSEN ET AL.

**Art Unit**

1637

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to papers filed 12/04/2008.
2. ☒ The allowed claim(s) is/are 1,3,4,10 and 12-17.
3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☒ None of the:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_.

### **EXAMINER'S AMENDMENT**

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Martin Fessenmaier on 12/16/2008.

The application has been amended as follows:

In claim 3, replace the text "...an HPV gene other than the HPV E1 gene." with "...an HPV gene in addition to the HPV E1 gene."

In claims 10 and 15, replace the text "...belong to different ones of risk clusters." with "...belong to different HPV risk types."

In claims 12 and 13, replace the text "The method of claim 2..." with "The method of claim 1..."

The following is an examiner's statement of reasons for allowance: The claims as amended recite nucleic acid probes or the use thereof in the claimed methods, wherein the probes are selected from among SEQ ID NO:24 to 59. Each of these probes comprises at the 5' end a "spacer" sequence: TTTTCTTTTCTTTTC. While it was known in the art to employ non-specific nucleotide spacers for attaching specific nucleic acid probes to a solid phase, there is no teaching or suggestion for this particular spacer, nor any rationale for selecting this particular spacer out of the uncountable

number of possible lengths and sequences of spacer. Furthermore, Applicant's specification at page 12, states that the nucleotide composition of the spacer "need to be selected in such a way that no cross hybridization occurs with other relevant DNA fragments in the assay." To avoid cross hybridization was also known in the art. Since HPV is a human pathogen, human DNA would reasonably be expected to be present in the sample being assayed.

In fact, TTTTCTTTTCTTTTC is found within the human genome. It is found within a short tandem repeat (STR) in the first intron of human CD4 gene (which is on chromosome 12) (Edwards reference, page 4791; note that a repetition of at least 4 CTTT units produces the sequence of the Applicant's spacer):

*Source and Description of Clone:* Partial sequencing of an approximately 15 kb lambda insert (lambda hg1) containing exons 1-3 of the human CD4 gene revealed a tract of 12 CTTT's. The sequences flanking the pentanucleotide repeat (CTTT)<sub>n</sub> were then used to design PCR primers that amplified a 113 base pair fragment from lambda hg1.

*Primer Sequences:*

5'-TTGGAGTCGCAAGCTGAAGTAGC-3' (CTTT strand),  
5'-GCCTGAGTGACAGAGTGAGAACC-3' (AAAAG strand)

*Polymorphism:* Allelic fragments in 5 bp intervals from 88 to 128 bp.

*Frequencies:* (a) in 100 unrelated Caucasians, (b) in 14 unrelated North American Blacks:

Allele (bp)	Freq.(a)	Freq.(b)	Allele (bp)	Freq.(a)	Freq.(b)
A8 88	0.365	0.286	A4 108	0.300	0.036
A7 93	0.295	0.214	A3 113	0.025	0.250
A6 98	0.005	0.107	A2 118	0.005	0.036
A5 103	0.005	0.036	A1 128	0.000	0.036

It is also an STR on the human Y chromosome, where there can be from 8-12 repeats of TTTTC (Butler reference, Table 14.8.3):

Table 14.8.3 Characteristics of common Y-chromosome STR markers

STR Marker	Position (Mb)*	Repeat Motif	Allele Range*	PCR Product Size (Kb)	STR diversity*
DYS19	9.44	TAGA	10-19	232-268 bp (PPY)	0.498
DYS385 a/b	20.00, 20.04	GAAA	7-25	243-315 bp (PPY)	0.838
DYS389I/II	13.92	TCG TCTA	10-15 / 24-34	148-168 bp / 256-296 bp (PPY)	0.538/ 0.675
DYS390	16.52	TCTA TCTG	18-27	191-227 bp (PPY)	0.701
DYS391	13.41	TCTA	6-13	90-118 bp (PPY)	0.552
DYS392	21.78	TAT	7-18	294-327 bp (PPY)	0.596
DYS393	3.04	AGAT	8-16	104-136 bp (PPY)	0.363
DYS437	13.78	TCTA	13-17	183-199 bp (PPY)	0.583
DYS438	14.25	TTTTC	8-12	101-121 bp (PPY)	0.594
DYS439	15.85	AGAT	8-15	203-231 bp (PPY)	0.639

\*Positions determined along human genome reference sequence in Jan 2003 using BLAT (see Butler 2003)

\*Ranges are calculated from kit allelic ladders and do not represent the full range of alleles observed in world populations

\*Calculated from 244 Caucasian males (Schouke et al. 2003)

The presence of Applicant's spacer sequence within the human genome not only fails to provide a rationale to use that sequence as a spacer, but actually provides a rationale *not* to use that sequence.

Applicant is reminded that a certified copy of the foreign priority document, application 02076494.0, has not been provided.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAMUEL WOOLWINE whose telephone number is (571)272-1144. The examiner can normally be reached on Mon-Fri 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel Woolwine/  
Examiner, Art Unit 1637

/GARY BENZION/  
Supervisory Patent Examiner, Art Unit 1637